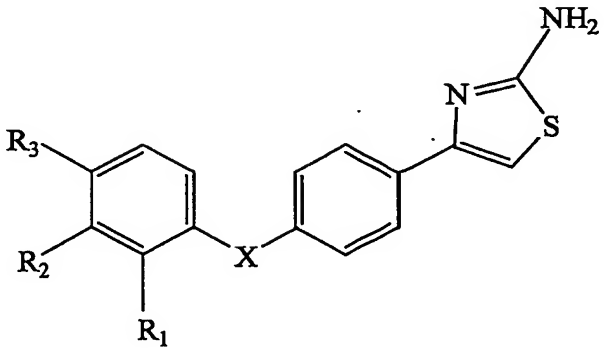
Claims

What is claimed is:

1. A compound having the general structural formula of structure I



I

wherein said compound is selected from the group consisting of substituted 4-aryloxy and 4-arylsulfanyl-phenyl-2-aminothiazoles comprising structure I, further wherein said compound has anti-cancer activity.

2. The compound of claim 1, wherein:

X is selected from the group consisting of O, S, and NH; and

R_1, R_2, and R_3 are independently selected from the group consisting of H, halo, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, aryl, -O-aryl and $(CO)OR_4$; and

R_4 is H or $(C_1\text{-}C_4)$alkyl; and

pharmaceutically acceptable salts thereof.

3. The compound of claim 1, wherein:

X is O or S; and

R_1 is H; and

R_2 and R_3 are independently selected from the group consisting of H, Cl, $(C_1\text{-}C_2)$alkyl, $(C_1\text{-}C_2)$alkoxy, phenyl, -O-phenyl and $(CO)OCH_2CH_3$; and

pharmaceutically acceptable salts thereof.

4. The compound of claim 1, wherein:

X is O or S; and

R_1 is H; and

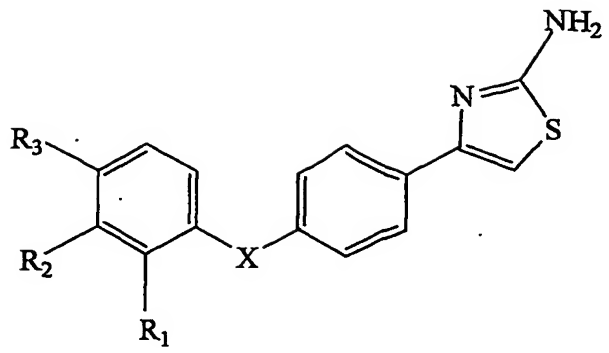
R_2 and R_3 are independently selected from the group consisting of H, Cl, (C_1-C_2)alkyl, (C_1-C_2)alkoxy, phenyl, -O-phenyl and $(CO)OCH_2CH_3$; and

pharmaceutically acceptable salts thereof.

5. A compound according to claim 1 selected from the group consisting of 4-(4'-Phenoxyphenyl)-thiazol-2-yl ammonium iodide (16); 4-[4'-(4-Chlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (17); 4-[4-(3'-Chlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (18); 4-[4-(2'-Chlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (19); 4-[4'-(3,4-Dichlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (20); 4-[4'-(4-Methoxyphenoxy)-phenyl]-thiazol-2-yl ammonium iodide (21); 4-[4'-(*p*-Toluoxy)phenyl]-thiazol-2-yl ammonium iodide (22); 4-[4'-(Biphenyl-4-yloxy)-phenyl]-thiazol-2-yl ammonium iodide (23); 4-[4'-(4-Phenoxy-phenoxy)-phenyl]-thiazol-2-yl ammonium iodide (24); 4-[4-(3'-Ethoxycarbonyl-phenoxy)-phenyl]-thiazol-2-yl ammonium iodide (25); 4-(4'-Phenylsulfanyl-phenyl)-thiazol-2-yl ammonium iodide (26); 4-[4-(4'-Chloro-phenylsulfanyl)-phenyl]-thiazol-2-yl ammonium iodide (27); 4-[4-(3',4'-Dichloro-phenylsulfanyl)-phenyl]-thiazol-2-yl ammonium iodide (28); 4-[4-(4'-Methoxy-phenylsulfanyl)-phenyl]-thiazol-2-yl ammonium iodide (29); and 4-(4'-*p*-Tolylsulfanyl-phenyl)-thiazol-2-yl ammonium iodide (30).

6. A pharmaceutical composition comprising at least one compound according to claims 1, 2, 3, 4, or 5, and a pharmaceutically acceptable carrier.

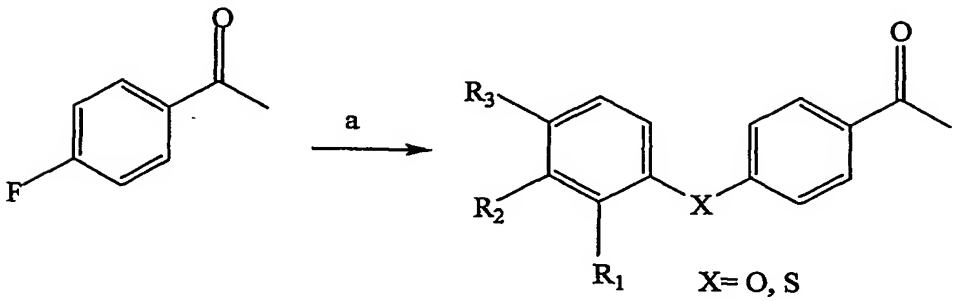
7. A method of preparing substituted 4-aryloxy and 4- arylsulfanyl-phenyl-2-aminothiazole compounds with anti-cancer activity comprising the structural formula of structure I:



I

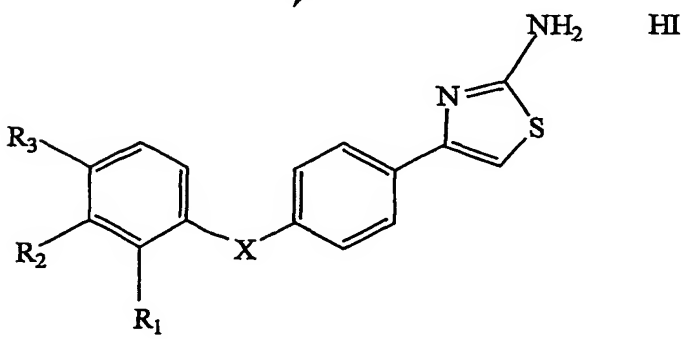
said method comprising preparing said compound according to scheme 1:

Scheme 1



X= O, S

2-15



HI

X= O, S

17-30

8. A compound prepared by the method of claim 7, wherein:

X is selected from the group consisting of O, S, and NH; and

R_1, R_2, and R_3 are independently selected from the group consisting of H, halo, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, aryl, -O-aryl and $(CO)OR_4$; and

R_4 is H or $(C_1\text{-}C_4)$alkyl; and

pharmaceutically acceptable salts thereof.

9. A compound prepared by the method of claim 7, wherein:

X is O or S; and

R_1 is H; and

R_2 and R_3 are independently selected from the group consisting of H, Cl, $(C_1\text{-}C_2)$alkyl, $(C_1\text{-}C_2)$alkoxy, phenyl, -O-phenyl and $(CO)OCH_2CH_3$; and

pharmaceutically acceptable salts thereof.

10. A compound prepared by the method of claim 7, wherein:

X is O or S; and

R_1 is H; and

R_2 and R_3 are independently selected from the group consisting of H, Cl, $(C_1\text{-}C_2)$alkyl, $(C_1\text{-}C_2)$alkoxy, phenyl, -O-phenyl and $(CO)OCH_2CH_3$; and

pharmaceutically acceptable salts thereof.

11. The method of claim 7, wherein a compound prepared by said method is selected from the group consisting of:

4-(4'-Phenoxyphenyl)-thiazol-2-yl ammonium iodide (16); 4-[4'-(4-Chlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (17); 4-[4-(3'-Chlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (18); 4-[4-(2'-Chlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (19); 4-[4'-(3,4-Dichlorophenoxy)-phenyl]-thiazol-2-yl ammonium iodide (20); 4-[4'-(4-Methoxyphenoxy)-phenyl]-thiazol-2-yl ammonium iodide (21); 4-[4'-(*p*-Toluoxy)phenyl]-thiazol-2-yl ammonium iodide (22); 4-[4'-(Biphenyl-4-yloxy)-phenyl]-thiazol-2-yl ammonium iodide (23); 4-[4'-(4-Phenoxy-phenoxy)-phenyl]-

thiazol-2-yl ammonium iodide (24); 4-[4-(3'-Ethoxycarbonyl-phenoxy)-phenyl]-thiazol-2-yl ammonium iodide (25); 4-(4'-Phenylsulfanyl-phenyl)-thiazol-2-yl ammonium iodide (26); 4-[4-(4'-Chloro-phenylsulfanyl)-phenyl]-thiazol-2-yl ammonium iodide (27); 4-[4-(3',4'-Dichloro-phenylsulfanyl)-phenyl]-thiazol-2-yl ammonium iodide (28); 4-[4-(4'-Methoxy-phenylsulfanyl)-phenyl]-thiazol-2-yl ammonium iodide (29); and 4-(4'-*p*-Tolylsulfanyl-phenyl)-thiazol-2-yl ammonium iodide (30).

12. A method of treating cancer in a subject in need thereof, said method comprising administering to said subject an effective amount of a pharmaceutical composition comprising at least one compound according to claims 1, 2, 3, 4, or 5, or pharmaceutically acceptable salts thereof.

13. The method of claim 12, wherein said cancer is selected from the group consisting of breast cancer, leukemia, non-small cell lung cancer, colon cancer, cancer of the central nervous system, melanoma, ovarian cancer, renal cancer, and prostate cancer.

14. The method of claim 12, wherein said breast cancer is selected from the group consisting of estrogen receptor positive, estrogen receptor negative, and adriamycin-resistant breast cancer.

15. The method of claim 12, wherein said composition is administered intravenously.

16. The method of claim 12, wherein said composition is administered intra-tumorally.

17. The method of claim 12, wherein said subject is a human.

18. A method of inhibiting proliferation of cancer cells, said method comprising contacting said cells with a composition comprising at least one compound of claims 1, 2, 3, 4, or 5.

19. The method of claim 18, wherein said cancer cell is selected from the group consisting of breast cancer, leukemia, non-small cell lung cancer, colon cancer, cancer of the central nervous system, melanoma, ovarian cancer, renal cancer, and prostate cancer cells.

20. The method of claim 18, wherein said breast cancer cell is selected from the group consisting of estrogen receptor positive, estrogen receptor negative, and adriamycin-resistant breast cancer cells.

21. A kit for administering a compound which has anti-cancer activity to a subject in need of such treatment, said kit comprising a pharmaceutical composition comprising at least one compound of claims 1, 2, 3, 4, or 5, an applicator, and an instructional material for the use thereof.